ABSTRACT OF THE INVENTION

The present invention describes methods of producing milligram quantities of three forms of purified Stat1 protein from recombinant DNA constructs. In addition, the Stat proteins may be isolated in their phosphorylated or nonphosphorylated forms (Tyr 701). The proteins can be produced in baculovirus infected insect cells, or *E.* coli. A compact domain in the amino terminus of Stat1α was isolated and found to enhance DNA binding due to its ability to interact with a neighboring Stat protein. A relatively protease-resistant recombinant truncated form of the Stat protein was isolated in 40-50 mg quantities. Purification of the Stat proteins were performed after modifying specific cysteine residues of the Stat proteins to prevent aggregation. Activated EGF-receptor partially purified from membranes by immunoprecipitation was shown to be capable of *in vitro* catalysis of the phosphorylation of the tyrosine residue of Stat1 known to be phosphorylated *in vivo*. Techniques are enclosed to separate the phosphorylated from the nonphosphorylated Stat proteins. The techniques disclosed are general for Stat proteins and may be used to isolate large quantities of purified Stat 2, 3, 4, 5A, 5B and 6. Methods for using purified Stat proteins, truncated Stat proteins, or Stat N-terminal fragments for drug discovery are also disclosed.